The Medical Laboratory Evaluation of a Child Diagnosed With Autism Spectrum Disorder

Confirmation of an autism spectrum disorder (ASD) diagnosis is usually done by a pediatric subspecialist or ideally by a team of ASD or developmental specialists. Although several strategies may be used, all depend on confirmation of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, criteria. The Autism Diagnostic Interview-Revised and Autism Diagnostic Observation Schedule are used in most research settings to confirm the presence of these criteria, but expertise in these assessments is often not available in clinical settings. Thus, the specialist(s) must use a battery of evaluation instruments to assess social and language skills and presence of atypical ASD behaviors. Additionally, a thorough history (including health, developmental, behavioral, and family histories), a physical examination, and some evaluation of the child's overall level of functioning (cognitive, adaptive, and motor skills) are also very important. Finally, one should also assess the family's resources and coping strategies.

Once the diagnosis of ASD is confirmed by a specialist or team of specialists, the pediatrician plays an important role in the medical evaluation. Although medical investigations include a search for conditions that are known to play an etiologic role in ASD (eg, fragile X syndrome), they may also be directed at determining the presence of a coexisting medical condition (eg, seizures, hearing loss). Other factors, such as the availability of local technology and ASD diagnostic teams and/or pediatric subspecialists (developmental pediatricians, neurologists, geneticists, or psychiatrists) with an interest in ASD, will also affect the primary care pediatrician's role. Some managed care systems may require the primary care pediatrician to order or approve laboratory tests.

An extensive medical laboratory workup is not currently supported by research. This may change as newer technology becomes clinically available and is evaluated. The yield of etiologic evaluation in children without coexisting mental retardation (MR), dysmorphic features, and/or a family history of MR is extremely low. Thus, a thorough laboratory investigation is not recommended in all children with ASDs. However, the clinician must obtain a detailed history (including a 3-generation pedigree) and conduct a thorough physical examination (including a Wood lamp evaluation of the skin) to determine if there are any clinical indications for specific laboratory investigations.

The American Academy of Pediatrics policy statement and accompanying technical report on ASDs\(^1,2\) suggest a tiered approach for the etiologic workup of a child with ASD.

### Level 1

An audiologic evaluation should be done in all children with language delay, including those with ASDs. School screening may suffice in older children who can cooperate.

### Level 2

High-resolution chromosomes (650 bands) and a DNA study for fragile X syndrome should be done in all children with ASDs who have coexisting global developmental delays (GDDs) or, in older children, coexisting MR in addition to ASD. The clinician may want to also consider a fluorescence in situ hybridization (FISH) study to determine the presence of a possible duplication of 15q and/or a methyl CpG binding protein 2 (Rett syndrome) (MECP2) study in females who present with regression.
Level 3

Additional laboratory investigations should be considered when specific indications are identified by history or physical examination. When available, interdisciplinary ASD diagnostic teams with pediatric subspecialty team members will determine the extent of the medical evaluation as part of the comprehensive evaluation. When this is not the case, the primary care pediatrician, depending on his or her level of comfort, should consider making referrals to a developmental pediatrician, child neurologist, or clinical geneticist to assist with a Level 3 search.

- Children should undergo a quantitative plasma amino acid assay to rule out phenylketonuria when it is suspected by history or physical evaluation and newborn screening results are not available.
- Children with coexisting GDD/MR may require additional diagnostic testing with genetic consultation (eg, MECP2, FISH).
- Children with regression, microcephaly, midline facial defects, neurocutaneous lesions (with or without the help of a Wood lamp), abnormalities on neurologic examination, a history of seizures, or a suspicion of subclinical seizures should be considered for magnetic resonance imaging (MRI) and an electroencephalogram (EEG). Screening EEGs on all children with ASDs are not currently recommended. Isolated macrocephaly is not, in itself, an indication for an MRI.
- Children with cyclic vomiting, hypotonia, lethargy (especially when associated with mild illnesses), poor growth, unusual odors, multiple organ involvement, ataxia or other movement disorder, or evidence of a storage disease (eg, coarse features) should be evaluated by a metabolic specialist or clinical geneticist.
- Although lead toxicity is not felt to cause ASD, it can have a detrimental effect on learning and cognition that may indirectly intensify ASD symptoms. Children with pica, especially living in at-risk environments, should be monitored with ongoing blood lead levels as long as pica persists. Serum ferritin may also be indicated.

Note: There is no evidence that indicates hair analysis, micronutrient levels, intestinal permeability studies, stool analyses, urinary peptides, or mercury levels are helpful. Although functional neuroimaging studies have been helpful in mapping brain areas that function atypically in various processing tasks, they are not clinically indicated in the etiologic workup of a child with ASD.

Children with ASDs can manifest a variety of coexisting disorders such as seizures, gastrointestinal, and sleep. These conditions may also cause an acute change in behavior. See the Physician Fact Sheets and Family Handouts sections of this toolkit for more information.

References
